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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/523,102	03/10/2000	Erwin Si	03654.0255	4492

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EXAMINER	
SAUCIER, SANDRA E	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 10/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/523,102	SI ET AL.	
	Examiner	Art Unit	
	Sandra Saucier	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42 and 67-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-42 and 67-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 March 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/6/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-42, 67-70 are pending and are considered on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

The amendments to the specification submitted 8/6/04 has not been entered and is objected to because of the following informalities:

On the first page of the amendments to the specification, the formula at the bottom of the page has been transposed with the sentence appearing directly above it. Please check the US Patent from which the disclosure has been incorporated.

Appropriate correction is required and the amendments to the specification will be entered upon correction.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-42 and 67-70 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable

over claims 1-11, 13, 30-37, 39 of copending Application No. 09/648446. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are directed to the same method of topically applying a therapeutic agent (batimastat) to the eye for treatment of posterior segment of the eye (retina).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112
INDEFINITE

Claims 67 and 69 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear from the construction of the claim what is excluded from the composition since it both comprises a polymeric agent to which other compounds may be added and consists essentially of batimastat. The metes and bounds are not clear. A composition should "consist essentially of" not merely a component of that composition. it is the composition as a whole which excludes components added which materially change its properties.

Claim Rejections - 35 USC § 102

Claims 7-12, 14, 23-30, 32, 38-42, 69 and 70 are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,767,153.

The claims are directed to the one step method of preventing retinal neovascularization by topically administering to the eye a composition comprising 0.01-3% w/w batimastat of the claim specific formula and a polymeric suspension agent. The mammal which is the recipient of this administration is a mammal that is susceptible to developing retinal neovascularization. Other claims are broader in some aspect of the composition limitations.

US 5,767,153 teaches the topical administration to a recipient of a composition comprising batimastat (0.3 weight %) and polycarbophil (1.15 weight %). Since everyone is susceptible to developing retinal neovascularization by developing the diseases of the retina and/or traumatic ocular insults as described on page 1 of the instant specification, and no specific type of recipient is required by the claims, the recipient is interpreted to be the same as the recipient of the claims. As the

composition administered is the same (batimastat and polycarbophil), the concentrations of the components of the composition is the same and the patient required is the same, the inherent result of the one method step would be the same, that is prevention of retinal neovascularization.

" To invalidate a patent by anticipation, a prior art reference normally needs to disclose each and every limitation of the claim. See Standard Havens Prods., Inc. v. Gencor Indus., Inc., 953 F.2d 1360, 1369, 21 USPQ2d 1321, 1328 (Fed. Cir. 1991). However, a prior art reference may anticipate when the claim limitation or limitations not expressly found in that reference are nonetheless inherent in it. See id.; Verdegaal Bros., Inc. v. Union Oil Co. of Cal., 814 F.2d 628, 630, 2 USPQ2d 1051,1053 (Fed. Cir. 1987). Under the principles of inherency, if the prior art necessarily functions in accordance with, or includes, the claimed limitations, it anticipates. See In re King, 801 F.2d 1324, 1326, 231 USPQ 136, 138 (Fed. Cir. 1986). Inherency is not necessarily coterminous with the knowledge of those of ordinary skill in the art. See Titanium Metals, 778 F.2d at 780. Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art. See id. at 782. However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. See id. at 782 ("Congress has not seen fit to permit the patenting of an old [composition], known to others . . . , by one who has discovered its . . . useful properties."); Verdegaal Bros., 814 F.2d at 633.

This court's decision in Titanium Metals illustrates these principles. See Titanium Metals, 778 F.2d at 775. In Titanium Metals, the patent applicants sought a patent for a titanium alloy containing various ranges of nickel, molybdenum, iron, and titanium. The claims also required that the alloy be "characterized by good corrosion resistance in hot brine environments." Titanium Metals, 778 F.2d at 776. A prior art reference disclosed a titanium alloy falling within the claimed ranges, but did not disclose any corrosion-resistant properties. This court affirmed a decision of the PTO Board of Appeals finding the claimed invention unpatentable as anticipated. This court concluded that the claimed alloy was not novel, noting that "it is immaterial, on the issue of their novelty, what inherent properties the alloys have or whether these applicants discovered certain inherent properties." Id. at 782. This same reasoning holds true when it is not a property, but an ingredient, which is inherently contained in the prior art. The public remains free to make, use, or sell prior art compositions or

processes, regardless of whether or not they understand their complete makeup or the underlying scientific principles which allow them to operate. The doctrine of anticipation by inherency, among other doctrines, enforces that basic principle." See Atlas Powder Co. v. IRECO Inc. 51 USPQ2d 1943 (Fed. Cir. 1999).

Thus, a reference may be anticipatory if it discloses every limitation of the claimed invention either explicitly or inherently. A reference includes an inherent characteristic if that characteristic is the "natural result" flowing from the reference's explicitly explicated limitations. Continental Can Co. USA, Inc. v. Monsanto Co., 948 F.2d 1264, 1269, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991).

Claim Rejections - 35 USC § 103

Claims 1-42, 67-70 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,767,153 [A] in view of WO 97/41844.

The claims are directed to a one step method of treating or preventing retinal neovascularization in an animal comprising topically administering a composition comprising (0.01-3% w/w) batimastat and in some of the claims, a polymeric suspension agent, particularly polycarbophil.

The references are relied upon as explained below.

US 5,767,153 discloses a composition comprising 0.3% batimastat and 1.15% polycarbophil useful for topical ophthalmic administration, (col. 2, l.7 and example 7). It teaches that inclusion of medicaments such as batimastat in combination with polycarbophil increases its bioavailability to the target tissue in the eye (col. 2, ls. 19-21).

The reference lacks the disclosure of use of the composition of polycarbophil and batimastat for the treatment of retinal neovascularization.

WO 97/41844 discloses that batimastat is an angiostatic agent (Table 1) and as such is effective in compositions for the treatment of diseases where neovascularization arises such as diabetic retinopathies, proliferative virtreoretinopathies and other diseases (page 1, second paragraph and page 5, table 1). Compositions comprising metalloproteinase inhibitors such as batimastat, which is a preferred angiostatic agent (page 19, l. 9) are in topical ophthalmic formulations (claim 20). The compositions may be used to prevent retinal neovascularization (page 20, l. 11).

The substitution of the composition of batimastat and polycarbophil disclosed in US 5,767,153 for the batimastat composition taught in the topical ocular treatment method of WO 97/41844 would have been obvious because batimastat is known to be useful to treat retinal neovascularization as taught in '844 and the formulation of batimastat with polycarbophil as a suspension agent is taught in '153 to be particularly advantageous in terms of delivering a sustained dosage of a sparingly water soluble active ingredient such as batimastat over time.

One of ordinary skill in the art would have been motivated at the time of invention to substitute a composition of batimastat for a composition of batimastat and polycarbophil to treat retinal neovascularization in order to obtain the results as suggested by the references with a reasonable expectation of success. The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

Response to Arguments

Applicants argue that '844 fails to teach the treatment of retinal neovascularization by topical administration of the compounds recited in the claims to the eye. This is true, as the reference is not an anticipatory one, but merely renders the claimed method obvious. The reference lacks the combination of the compounds of batimastat type compound and polycarbophil. It does have a formulation which includes a polymer and an angiostatic agent, however, see Example 1, where the polymer tyloxapol is used in the formulation of a topical ocular medicament.

Applicants argue that nothing in the references would suggest to the skilled artisan that the compounds set forth in the claims would cross the sclera and reach the retina.

Please see Example 1 where it is stated that the ocular topical composition is to be used for controlling ocular neovascularization. On page 2, line 7, it is stated that "the most threatening ocular neovascular diseases are those which involve the retina. For example, many diabetic patients develop a retinopathy...". This appears to be a strong suggestion to administer a compound of formula I and a matrix metalloprotease inhibitor otherwise known as an angiostatic compound, such as betimastat on page 19, ls. 9 and 27 to treat diabetic retinopathy, for example, as taught on page 20, l. 6.

The one step method of topically administering the composition is the same as suggested by the reference. The reference does not have to show that the compound crosses the sclera to reach the retina, as the one step claim is the same as the process suggested by the reference. Applicants allege that Example 1 is directed to topical combination compositions indication as useful for controlling ocular neovascularizations of tissue that do not include treatment of the retina. This allegation is merely an argument of counsel and is not substantiated by any teaching in the cited WO 97/41844 document.

Applicants argue that '844 teaches away from the topical application of batimastat for treatment of retinal disorders, and that it teaches the topical administration of batimastat for treatment of directly accessible tissues for pytergium, hyperderatosis, cheloid and polyp formation on page 24. In rebuttal, it is well established that a reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. The reference of '844 does not state that a topical application of batimastat is not effective for treatment of the retina and in fact, teaches in Examples 1 and 2, topical composition useful for controlling ocular neovascularization. The term, "ocular" includes the retina.

Applicants continue to cite Geroski *et al.* to bolster their argument that there is no reasonable expectation of success in the topical application of batimastat/polymer for treatment of retinal angiogenisis. However, Geroski *et al.* do not teach that there is no reasonable expectation of success, but that the topical administration of compounds to the eye typically does not yield therapeutic drug levels in the ...retina..., but that **topical formulations remain effective because the very high concentrations of drugs that are administered**." (first column, end of first paragraph). The reference goes on to suggest that recent advances in drug delivery such as polymeric gels will provide new topical drug therapeutics. This is exactly what the cited prior art teaches, the special combination of batimastat with a polycarbophil polymer which according to the primary reference of US '153 enhances the bioavailability of the combination when employed in a topical ophthalmic method. As the claimed method is a one step method of topical ocular administering of polycarbophil/batimastat and the prior art is considered to suggest such a treatment for retinal neovascularization, the claims are still considered to be obvious.

Applicants have argued that penetration to the retinal tissue from topical ocular administration is difficult and that the references provided by the examiner which show that the topical ocular administration of a drug has an effect on the retina do not demonstrate that the drug penetrated the sclera as opposed to other tissues through which the drugs might exert their influence. Therefore, the references fail to demonstrate that there is a reasonable expectation that the compounds recited in the claims will reach the retina when topically administered. Please note that the claims are directed to a one step method of topically administering the claim specific composition to the retina. This appears to be the same method as discussed in the references provided by the examiner to show the state of the art regarding treatment of the retina by topical ocular administration of drugs. In short, it is known in the prior art to treat the retina by topical ocular administration of a drug and that, therefore, the drug MUST reach the retina, because the drug's expected effect is seen to be expressed in the retinal tissue.

Please note that applicants' example 3 is not a working example, but merely a prophetic example or paper example of how an experiment will be carried out. See MPEP 608.01(p) II. Thus, Figure 5 which is discussed by applicants, in the response filed 5/26/04 does not necessarily appear to be actual data from a working example. Further, no explanation in the body of the specification is given for where the batimastat concentration was measured as diagrammed in the Y axis nor is there an indication of what a therapeutically effective dosage at the retina might be in Figure 5. Figure 5 is, therefore, not persuasive because it is not considered to be a working example and it is not clearly explained.

With regard to claim 68, the transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention. In re Herz , 537 F.2d 549, 551 - 52, 190 USPQ 461, 463 (CCPA 1976)(emphasis in original)(Prior art hydraulic fluid required a dispersant which appellants argued was excluded from claims limited to a functional fluid "consisting essentially of" certain components. In finding the claims did not exclude the prior art dispersant, the court noted that appellants' specification indicated the claimed composition can contain any well - known additive such as a dispersant, and there was no evidence that the presence of a dispersant would materially affect the basic and novel characteristic of the claimed invention. The prior art composition had the same basic and novel characteristic (increased oxidation resistance) as well

as additional enhanced detergent and dispersant characteristics.). See also Atlas Powder Co. v. E.I. duPont de Nemours & Co. , 750 F.2d 1569, 224 USPQ 409 (Fed. Cir. 1984); In re Janakirama - Rao, 317 F.2d 951, 137 USPQ 893 (CCPA 1963); Water Technologies Corp. v. Calco, Ltd ., 850 F.2d 660, 7 USPQ2d 1097 (Fed. Cir. 1988).

When an applicant contends that additional steps or materials in the prior art are excluded by the recitation of "consisting essentially of," applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention. In re De Lajarte, 337 F.2d 870, 143 USPQ 256 (CCPA 1964). See also Ex parte Hoffman, 12 USPQ2d 1061, 1063 - 64 (Bd. Pat. App. & Inter. 1989)("Although 'consisting essentially of' is typically used and defined in the context of compositions of matter, we find nothing intrinsically wrong with the use of such language as a modifier of method steps . . . [rendering] the claim open only for the inclusion of steps which do not materially affect the basic and novel characteristics of the claimed method. To determine the steps included versus excluded the claim must be read in light of the specification . . . . [I]t is an applicant's burden to establish that a step practiced in a prior art method is excluded from his claims by 'consisting essentially of' language.").

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is 571-272-0922. The examiner can normally be reached on Monday, Tuesday, Wednesday.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sandra Saucier
Primary Examiner